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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,018	07/07/2003	Ursula-Henrike Wienhues	2923-543	8627

6449 7590 08/23/2007

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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
08/23/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/613,018	WIENHUES ET AL.	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2007 and 19 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-22* is/are pending in the application.

4a) Of the above claim(s) *5,8,13 and 15-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,7,9-12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/776,188.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 25, 2007 has been entered.

Status of the Claims

2. The amendment to the claims received on September 6, 2006 canceled claim 2 and amended claim 1.

The amendment to the claims received on April 25, 2007 canceled claims 23-24 and amended claim 1.

Claims 1 and 3-22 are currently pending.

Claims 1, 3-4, 6-7, 9-12, and 14 are currently under consideration.

Rejoinder

3. Applicants state that claims 5, 8, 13, and 15-22 may be subject to rejoinder if claim 1 becomes allowable. However, only claims 5, 8, 13, 15, and 19-22 are subject to rejoinder (i.e. non-elected species of Group I). Claims 16-18 are product claims of Group II and are not subject to rejoiner.

Applicants are respectfully reminded that where applicants elect claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be

rejoined in accordance with the provisions of MPEP § 821.04. However, applicants have elected the process in the present application. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Invention as Claimed

4. A method for detection of an antibody against a pathogenic organism in a liquid sample wherein said pathogenic organism is selected form the group consisting of bacteria, viruses, and protozoa and the method comprising: (a) incubating the following: (1) the liquid sample, (2) a solid phase, (3) a first antigen for said antibody wherein the first antigen has at least one marker group and comprises multiple epitope regions, said epitope regions being identical in amino acid sequence, and (4) a second antigen for said antibody wherein the second antigen binds to the solid phase wherein said incubating is under conditions to obtain a complex comprising a solid phase-bound second antigen to which is bound the antibody and to which is bound the first antigen and (b) detecting said antibody by direct or indirect detection of the marker group on said solid phase wherein at least said first antigen is of formula $(P\text{-})_nT(\text{-}L)_n$ (Ia) or $T(\text{-}P\text{-}L_m)_n$ (Ib) wherein T is a carrier, P is a peptide comprising an epitope region wherein said epitope region is reactive with the antibody, L is the marker group or a group which binds to the solid phase, - is a covalent coupling, n is 2-40, and m is 1-10 and variations thereof.

Withdrawn Rejections

5. The rejection of claims 1, 3-4, 9-12, and 14 under 35 U.S.C. 103(a) as being unpatentable over Hashida et al., Diagnosis of HIV-1 Infection by Detection of Antibody IgG to HIV-1 Urine with Ultrasensitive Enzyme Immunoassay (Immune Complex Transfer Enzyme Immunoassay)

Using Recombinant Proteins as Antigens, Journal of Clinical Laboratory Analysis, 8(4): 237-246, 1994 and Formoso et al. WO 90/07119 published June 28, 1990 is withdrawn due to the claim amendments received on April 25, 2007 regarding the structure of the first antigen and utilizing a single solid phase.

6. The rejection of claims 6-7 under 35 U.S.C. 103(a) as being unpatentable over Hashida et al., Diagnosis of HIV-1 Infection by Detection of Antibody IgG to HIV-1 Urine with Ultrasensitive Enzyme Immunoassay (Immune Complex Transfer Enzyme Immunoassay) Using Recombinant Proteins as Antigens, Journal of Clinical Laboratory Analysis, 8(4): 237-246, 1994 and Formoso et al. WO 90/07119 published June 28, 1990 as applied to claims 1, 3-4, 9-12, and 14 above, and further in view of Watts et al. U.S. Patent 5,437,983 filed February 1, 1993 is withdrawn due to the claim amendments received on April 25, 2007 regarding the structure of the first antigen and utilizing a single solid phase.

New Rejections

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 3-4, 6-7, 9-12, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of ordinary skill in the art would not be able to determine the scope of the presently claimed invention. Claim 1 states that the first antigen has a marker group and multiple epitope regions that are identical in amino acid sequence (please refer to

section 3). "Has" is a transitional phrase which may be interpreted as opened or closed, thus it is unclear if the first antigen can only contain a marker and a multiepitope portion or if the first antigen can also contain other elements. Claim 1 also states that the first antigen is of formula $(P-)_nT(-L)_n$ (Ia) or $T(-P-L_m)_n$ (Ib) wherein L is a marker group or a group which binds to the solid phase and T is a carrier (please refer to section b). Applicants must clarify the structure of the first antigen. Therefore, is the marker of the first antigen optional (i.e. solid phase binding group can be substituted), can the first antigen have a carrier, can both the first and second antigens be bound to the solid support, etc.?

9. Claims 1, 3-4, 6-7, 9-12, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of ordinary skill in the art would not be able to determine the scope of the presently claimed invention. Claim 1 requires that the complex comprises a solid phase bound second antigen bound to antibody which is bound to a first antigen which has a marker group. However, claim 1 also requires detection of the marker group on the solid phase. Applicants must clarify the structure of the complex. For example, is the marker directly bound to the solid phase, is the marker indirectly bound to the solid phase (e.g. marker and solid phase separated by second antigen, antibody, and first antigen; marker separated from the solid phase by first antigen only, etc.), etc.?

10. Claims 1, 3-4, 6-7, 9-12, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. One of ordinary skill in the art would not be able to determine the scope of the presently claimed invention. Claim 1 requires that the second antigen binds to the solid phase. However, claim 1 also indicates that the second antigen can have a structure of formula $(P\text{-})_nT(\text{-}L)_n$ (Ia) or $T(\text{-}P\text{-}L_m)_n$ (Ib) wherein T is a carrier, P is a peptide comprising an epitope region wherein said epitope region is reactive with the antibody, L is the marker group or a group which binds to the solid phase, - is a covalent coupling, n is 2-40, and m is 1-10. Thus, the second antigen may or may not be directly bound to the solid support depending on the structure of the second antigen. Applicants must clarify the structure of the second antigen and how the second antigen is bound to the solid support. For example, is the second antigen directly bound to the solid support, is the second antigen bound to the solid support via a linker or carrier, etc.?

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1, 3-4, 6, 9, 12, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Flavell et al. U.S. Patent 5,618,533 filed December 10, 1993.

For present claim 1, Flavell et al. teach double antigen sandwich assays for detection of *B. burgdorferi* (i.e. bacteria) antibodies comprising (1) incubating patient sera (i.e. liquid sample), solid phase, antigen bound to support (i.e. second antigen), and a labeled antigen (i.e. first antigen with marker) wherein the antigens can be multimeric and coupled to a carrier and (2) detecting antigen and antibody binding in the bound state on the solid phase (please refer to the entire specification particularly abstract; columns 3-6 and 9-10).

For present claims 3-4, Flavell et al. teach antigens that are part of larger multimeric proteins comprising multiple copies of antigens and/or fusion proteins with repeated sequences of the same block of amino acids (please refer to the entire specification particularly column 5).

For present claim 6, Flavell et al. teach antigens that are part of larger multimeric proteins comprising multiple copies of antigens and/or fusion proteins with repeated sequences of the same block of amino acids (i.e. hapten coupled to antigen), flagellin antigens coupled to other *B. burgdorferi* antigens including OspA and OspB (i.e. haptens), coupled to carriers, and labeled anti-IgG or anti-IgM (i.e. binding partner labeled with a signal generating group) wherein the label can be detected (please refer to the entire specification particularly columns 5-6 and 9-10).

For present claim 9, Flavell et al. teach carriers (please refer to the entire specification particularly columns 6, 9).

For present claim 12, Flavell et al. teach recombinant antigens 35-46 amino acids in length (please refer to the entire specification particularly Figures 2, 4A, 4B; column 5; sequence listing).

For present claim 14, Flavell et al. teach recombinant antigens of 35+ amino acids in length which can be multimers (please refer to the entire specification particularly Figures 2, 4A, 4B; column 5; sequence listing).

Therefore, the presently claimed invention is anticipated by the teachings of Flavell et al.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1, 3-4, 6-7, 9-12, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rejman et al. EP 0 507 586 (supplied by applicants in IDS), Formoso et al. WO 90/07119 published June 28, 1990, and Watts et al. U.S. Patent 5,437,983 filed February 1, 1993.

For present claim 1, Rejman et al. teach immunoassay methods for detecting antibodies comprising (1) incubating a sample, a support, an antigen-small molecule conjugate (i.e. second antigen), and an antigen-signal generating means conjugate (i.e. first antigen with a marker; labeled antigen) wherein the support has a receptor for the small molecule (i.e. second antigen bound to support) and the labeled antigen can also have a small molecule and/or receptor (i.e. carrier) and (2) detection of the signal on the support (please refer to the entire specification particularly abstract; pages 2-4, 7).

For present claims 3-4, Rejman et al. teach that the first and second antigens can be the same (please refer to the entire specification particularly page 3).

For present claims 6-7, Rejman et al. teach direct and indirect labeling and detection of the bound antigen (please refer to the entire specification particularly pages 4-5).

For present claims 9-11, Rejman et al. teach small molecules/receptors (i.e. carrier) bound to antigens wherein the carrier can be antibody, Fab, polypeptide (please refer to the entire specification particularly pages 3-4).

However, Rejman et al. does not specifically teach multimers or the size of the antigens.

For present claims 3-4, Formoso et al. teach multimers and polymers of various peptides (e.g. antigens, epitopes, multiple epitope regions of identical amino acid sequence; please refer to entire specification particularly claims 2-9 and 11-18).

For present claims 12 and 14, Formoso et al. teach synthetic peptides conjugated through the C-terminus to a carrier protein which are typically about 5 to about 22 amino acids in length and preferably 11-20 amino acids or 15-17 amino acids in length (e.g. sequences of 6 to 50 amino acids; please refer to page 3, lines 22-32, page 4, lines 33-35, page 9, lines 24-36).

In addition, the elected species of SEQ ID No: 5 is taught by Formoso et al. including peptides of HIV-1 gp41 with the amino acid sequence of 1-15 of present SEQ ID NO:. 5 (please refer to claims 2 and 11). Furthermore, Formoso et al. teach that the carrier protein is preferably BSA, the peptides can be utilized in determining the presence of HIV-1 or HIV-2 antibodies in fluid samples, and that multiple peptides can be utilized in the ELISA, EIA, or RIA assays to determine the presence of HIV antibodies (please refer to pages 3-4 Summary of the Invention section and pages 8-17 Description of the Specific Embodiments section).

However, neither Rajman et al. nor Formoso et al. teach cardiotonic glycoside haptens and indirect detection via antibodies that bind the haptens.

For present claims 6-7, Watts et al. teach digoxigenin (e.g. cardiotonic glycosides) and antidigoxigenin antibody in binding assays with analytes and sbp or specific binding pairs and detecting signals (please refer to column 2, lines 1-18; column 3, lines 3-52; column 4, lines 15-35; column 5, lines 1-4; and Examples).

In addition, Watts et al. teach binding of sbps including antigens to labels to produce a signal producing system, utilizing beads as solid supports, performing the assay in a liquid medium, utilizing BSA, and screening for HIV related antibodies (please refer to column 4, lines 15-29; column 6, lines 41-67; column 7, lines 1-25, column 8, lines 9-51; column 9, lines 3-41; column 10, lines 22-31; column 11, lines 11-63).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for detection of viral antibodies taught by Rejman et al. with the shorter synthetic peptides in multimeric form taught by Formoso et al. and the digoxigenin and anti-digoxigenin detection system taught by Watts et al.

One having ordinary skill in the art would have been motivated to do this because Formoso et al. teach that synthetic peptides allow standardized antigen production, avoidance of nonspecificity resulting from contaminating proteins of *E. coli*, and reduced time of incorporating new antigens necessitated by mutation of HIV peptides which will improve tests for HIV specific antibodies (please refer to page 3, lines 7-20 of Formoso et al.) and Watts et al. teach that various detection and labeling systems can be utilized including enzymatic,

radioactive, and fluorimetric wherein one type of detection and labeling systems use is the digoxigenin and anti-digoxigenin detection system (please refer to column 1, lines 21-28).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method for detection of viral antibodies taught by Rejman et al. with the shorter synthetic peptides in multimeric form taught by Formoso et al. and the digoxigenin and anti-digoxigenin detection system taught by Watts et al. because Formoso et al. have shown the success of the screening and identification of antibodies using optimally immunoreactive peptides (please refer to page 11, lines 19-36 and page 12, lines 1-6 and Examples 1-20) and Watts et al. have shown the success of using the detection and labeling systems of digoxigenin and anti-digoxigenin detection system (col. 17, lines 17-47).

Therefore, the modification of the method for detection of viral antibodies taught by Rejman et al. with the shorter synthetic peptides in multimeric form taught by Formoso et al. and the digoxigenin and anti-digoxigenin detection system taught by Watts et al. render the instant claims *prima facie* obvious.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1, 3-4, 6-7, 9-12, and 14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31 (particularly claims 24-29) of U.S. Patent No. 5,804,371. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed method and the method claimed in U.S. Patent No. 5,804,371 are drawn to methods of determining antibody in a sample.

For present claims 1, 3-4, 6-7, 9-12, and 14, U.S. Patent No. 5,804,371 claims a method comprising incubating a second antigen bound to a solid phase with a liquid sample and a first antigen (i.e. peptide) that is at least 6 amino acids in length with a hapten (i.e. marker), a receptor (i.e. carrier, polypeptide), and/or a spacer (i.e. carrier, polylysine) and determining bound antibody (i.e. in sample) via detection wherein the hapten can be sterols, bile acids, sexual hormones, corticoids, etc. (please refer to claims 1-31 particularly claims 1, 13, and 24-29).

Conclusion

17. The art made of record and not relied upon is considered pertinent to applicant's disclosure. Hoesel et al. Journal of Immunological Methods 294: 101-110, 2004.

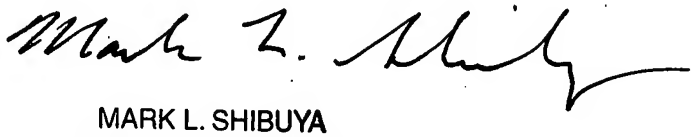
Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ADS
August 13, 2007



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